

described, each characterized by a unique sequence of mechanical, physical, chemical and/or enzymatic manipulations, which result in an acellular matrix that supposedly resembles the structure and composition (e.g., collagen and elastin contents) of the native tissue from which it was 5 derived. In general, acellular biological matrices have the advantage of possessing mechanical and three-dimensional structure properties similar to the native tissue from which they were derived and which, following tissue engineering, they are designed to replace. Allogenic and xenogenic matrices have provided a safe and effective biomaterial for numerous 10 medical applications, with minimal rejection [Furthmayr *et al.*, Int Rev Connect Tissue Res 7:61-99, 1976].

However, many *in-vivo* experiments utilizing acellular biological matrices did not produce the anticipated clinical outcome, mainly due to alterations in the matrix structure during the decellularization process.

15       The greatest challenge in tissue engineering is the replacement of whole organs with tissue engineered constructs having complex three-dimensional structures, such as kidney and liver. Tissue portions cannot be implanted in large volumes without a complex support system 20 that conserves the original structure and organization of the various cell types as in the native organ. Furthermore, if cells are located more than a few hundred micrometers from the nearest capillary, they will not survive due to diffusion limitations [Folkman *et al.*, J Exp Med 138: 745-749, 1973]. Constructs for implantation should, therefore, be fully vascularized prior to implantation. When implanted, constructs that are basically 25 two-dimensional, such as skin, blood vessel, bladder and ureter constructs contain cell-support matrices that enable nutrients and waste products to diffuse there across. Therefore, tissue engineered constructs that are no more than a few millimeters in thickness have a potential of staying viable once implanted. Constructs become vascularized in concert with the 30 expansion of cell mass.